

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY


(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

REC'D 14 MAR 2006

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Applicant's or agent's file reference 01710/1	FOR FURTHER ACTION See Form PCT/PEA/416	
International application No. PCT/IB2004/003238	International filing date (day/month/year) 04.10.2004 /	Priority date (day/month/year) 14.10.2003 /
International Patent Classification (IPC) or national classification and IPC INV. C07D403/04 C07D403/14 C07D407/14 C07D409/14 C07D413/14 A61K31/497 A61P29/00		
Applicant PHARMACIA CORPORATION et al. /		
<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 4 sheets, including this cover sheet. /</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input type="checkbox"/> sent to the applicant and to the International Bureau) a total of sheets, as follows:</p> <p><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>		
<p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the report</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input type="checkbox"/> Box No. VI Certain documents cited</p> <p><input type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input type="checkbox"/> Box No. VIII Certain observations on the international application</p>		
Date of submission of the demand 24.03.2005 /	Date of completion of this report 13.03.2006	
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Usuelli, A Telephone No. +49 89 2399-	



**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

International application No.
PCT/IB2004/003238

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
- ☐ international search (under Rules 12.3 and 23.1(b))
 - ☐ publication of the international application (under Rule 12.4)
 - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages

1-90 as originally filed

Claims, Numbers

1-14 as originally filed

- ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing
3. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):

* If item 4 applies, some or all of these sheets may be marked "superseded."

**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

International application No.
PCT/B2004/003238

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-14
	No: Claims	
Inventive step (IS)	Yes: Claims	1-14
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-14
	No: Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

**INTERNATIONAL PRELIMINARY
REPORT ON PATENTABILITY
(SEPARATE SHEET)**

International application No.

PCT/IB2004/003238

Re Item V

**Reasoned statement with regard to novelty, inventive step or industrial
applicability; citations and explanations supporting such statement**

1-Reference is made to the following documents cited in the search report:

- d1: WO 01/58890 A (BAXTER ANDREW ; BROUGH STEPHEN (GB); FAULL ALAN (GB); JOHNSTONE CRAIG) 16 August 2001 (2001-08-16)
- d2: WO 02/44153 A (SHIMADA MITSUYUKI ; BAYER AG (DE); ZIEGELBAUER KARL B (DE); UMEDA MASA) 6 June 2002 (2002-06-06)
- d3: WO 03/040131 A (HOFFMANN LA ROCHE) 15 May 2003 (2003-05-15)

2- Novelty

Present compounds differ from the compounds of d2 and d3 at least on account of the pyrazine ring. D1 discloses a pyrazine derivative (example 45) which differ from the compound of present formula (I) at least in that it lacks present group NHRa and X. Accordingly, present compounds of formula (I) can be regarded as novel. Since all the claims relate to these compounds, the requirements of Art. 33.2 PCT are met.

3- Inventive step

The applicant has set himself the task of providing novel IKK-2 inhibitors to be used in the treatment of inflammatory conditions.

Documents d1 to d3 relate to compounds having the same use of present compounds. Considering the chemical structures of the compounds disclosed in these documents, it is considered that d2 represents the closest state of the art.

The experimental results disclosed at page 90 of the description provide the evidence that present compounds indeed inhibit the IKK-2 kinase. Accordingly, the objective technical problem can be seen in the provision of further IKK-2 inhibitors to be used in the treatment of inflammatory conditions.

From the compounds of the closest state of the art, present compounds appear to differ at least on account of the heterocyclic ring and on account of the groups X and Rd.

Taking into account of these structural differences, it appears that the skilled person, even considering the teaching of d1 and d3 would not arrive to the present compounds in an obvious manner.

Accordingly, the requirements of Art. 33.3 PCT are met.